

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Jeffrey Hubbell, Jason Schense, Andreas Zisch, and Heike Hall

Serial No.: 10/650,509

Art Unit: 1651

Filed: August 27, 2003

Examiner: Leon B. Lankford, Jr.

For: *ENZYME-MEDIATED MODIFICATION OF FIBRIN FOR TISSUE
ENGINEERING*

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Commissioner for Patents
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REPLY BRIEF

Sir:

This is a Reply Brief to the Examiner's Answer mailed October 8, 2008, in the above-referenced application. Also submitted with this Reply Brief is a Request for Oral Hearing. The Commission is hereby authorized to charge \$1,080.00, the fee for a Request for Oral Hearing for a large entity, to Deposit Account No. 50-3129.

It is believed that no additional fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

(6) GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The issues on appeal are whether claims 1-5, 7, 9-14, 16-22, 26-30, 34, and 35 are patentable under the judicially created doctrine of nonstatutory double patenting in view claims 1-39 of U.S. Patent No. 6,331,422 to Hubbell, *et al.* ("the '422 patent"), claims 1-18 of U.S. Patent No. 6,607,740 to Hubbell, *et al.* ("the '740 patent"), 14-20 of U.S. Patent No. 7,247,609 to Lutolf, *et al.* ("the '609 patent"), and/or claims 1, 3-6, 9, 13, 14, 16-19, and 22-36 (now claims 1, 3-6, 9, 13, 14, 16-19, and 22-25) of U.S. Serial No. 10/323,046 by Hubbell, *et al.* ("the '046 application").

Page 4 of the Examiner's Answer mailed on October 8, 2008, indicated that claims 1-5, 7, 9-14, 16-22, 26-30, 34, and 35 are also finally rejected under the judicially created doctrine of non-statutory obviousness-type double patenting in view of claims 1-5 of U.S. Patent No. 6,894,022 to Hubbell, *et al.* ("the '022 patent"). However, page 3 of the Examiner's Answer does not list the '022 patent in the "Evidence Relied Upon" section. Furthermore, in the Advisory Action, the Examiner indicated that Applicants arguments had overcome the non-statutory obviousness-type double patenting rejection with respect to the '022 patent (Advisory Action mailed May 13, 2008, Continuation Sheet). Thus, it appears that the rejection over the '022 patent should not have been included in the Examiner's Answer. In a telephone conversation with the Examiner on December 1, 2008, the Examiner indicated that he would review the file and issue an appropriate correction to Section 9, the "Grounds of Rejection".

(7) ARGUMENTS

Appellants affirm all of the arguments made in the Appeal Brief.

(a) Rejection of claims 1-5, 7, 9-14, 16-22, 26-30, 34, and 35 under the judicially created doctrine of obviousness type double patenting.

(c) U.S. Patent No. 7,247,609 to Lutolf, et al. ("the '609 patent")

Claims 1-5, 7, 9-14, 16-22, 26-30, 34, and 35 were rejected under the judicially created doctrine of nonstatutory double patenting as obvious in view claims 14-20 of the '609 patent. Appellants respectfully traverse this rejection for at least the reasons set forth in the Appeal Brief and below.

(ii) Claims 1-5, 7, 9-14, 16-22, 26-30, 34, and 35 are not obvious in view of claims 14-20 of the '609 patent

M.P.E.P. § 804(B)(1) sets forth the standard for double patenting rejection as follows:

A double patenting rejection of the obviousness-type, if not based on an anticipation rationale, is "analogous to [a failure to meet] the nonobviousness requirement of 35 U.S.C. 103" except that the patent principally underlying the double patenting rejection is not considered prior art. *In re Braithwaite*, 379 F.2d 594, 154 USPQ 29 (CCPA 1967). Therefore, the analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. 103 obviousness determination. *In re Braat*, 937 F.2d 589, 19 USPQ2d 1289 (Fed. Cir. 1991); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Since the analysis employed in an obviousness-type double patenting determination parallels the guidelines for a 35 U.S.C. 103(a) rejection, the factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103 are employed when making an obvious-type double patenting analysis. These factual inquiries are summarized as follows:

- (A) Determine the scope and content of a patent claim relative to a claim in the application at issue;
- (B) Determine the differences between the scope and content of the patent claim as determined in (A) and the claim in the application at issue;
- (C) Determine the level of ordinary skill in the pertinent art; and
- (D) Evaluate any objective indicia of nonobviousness.

The conclusion of obviousness-type double patenting is made in light of these factual determinations.

The M.P.E.P. states that when an Examiner makes obviousness-type double patenting rejections, he should clearly explain:” (A) The differences between the inventions defined by the conflicting claims - a claim in the patent compared to a claim in the application; and (B) The reasons why a person of ordinary skill in the art would conclude that the invention defined in the claim at issue is >anticipated by, or< would have been an obvious variation of>,< the invention defined in a claim in the patent” (*Id.*).

Analysis

Contrary to the Guidelines set forth in the M.P.E.P., the Examiner has provided no reason why one of ordinary skill in the art would modify claims 14-20 of the '609 patent to arrive at the claims on Appeal.

Further, a modification of the claims 14-20 of the '609 patent to arrive at the present claims is impermissible for at least the following reasons:

1) such a modification would render claims 14-20 of the '609 patent unsatisfactory for their intended purpose; thus, there is no suggestion or motivation to make the proposed modification (*see* MPEP § 2143.01 (V));

2) such a modification would change the principle of operation of claims 14-20 of the '609 patent (*see* MPEP § 2143.01 (V)); and

3) claims 14-20 in the '609 patent teach away from claims 1-5, 7, 9-14, 16-22, 26-30, 34, and 35 of the present application (*see* MPEP § 2141.02).

(a) The scope of claims 14-20 of the '609 patent

Claims 14-20 of the '609 patent were summarized in the Appeal Brief (Appeal Brief, pages 11-12).

(b) Differences between claims 14-20 of the '609 patent and claims 1-5, 7, 9-14, 16-22, 26-30, 34, and 35 of the present application, and Evidence of Secondary Considerations.

Claims 1-5 of the present application

Claims 14-20 of the '609 patent do not define or make obvious the claimed composition comprising a matrix and a bidomain protein that comprises a polypeptide growth factor.

Claims 1-5 of the present application define a composition comprising a matrix and a bidomain protein or peptide having an amino acid sequence that comprises a transglutaminase substrate domain and a polypeptide growth factor, wherein the protein or peptide is covalently bound to the matrix by the transglutaminase substrate domain. Unlike claims 1-5 of the present application, claims 14-20 of the '609 patent require an enzymatic degradation site between the first domain (*i.e.* PTH) and the second domain (*i.e.* transglutaminase substrate domain).

The Examiner alleged that claims 14-20 of the '609 patent are a species of the claims in the present application (Examiner's Answer mailed October 8, 2008, page 4, para. 4). Appellants respectfully disagree. The present claims require a growth factor, while the claims 14-20 of the '609 patent require PTH.

The Examiner's allegation appears to be based on the election made by Appellants in the Response to Restriction Requirement filed on May 10, 2006, in which Appellants elected parathyroid hormone (PTH) for the domain containing a bioactive factor. In the Office Action mailed on August 29, 2006, the Examiner indicated that the elected species is free of the art, and that he had therefore searched the generic claim (Office Action mailed August 29, 2006, page 2, para. 3). However, in the Amendment and Response filed on December 29, 2006, independent claims 1, 10, 18, and 28, were amended to require a bidomain protein having an amino acid

sequence that comprises a transglutaminase domain and “a polypeptide growth factor”, instead of “a bioactive factor”, thus limiting the scope of the independent claims. Dependent claims 7, 9, 16, 17, 26, and 34 were amended to delete references to growth hormone and PTH. In the Office Action mailed on October 5, 2007, the Examiner entered the amendment into the record. Thus, the claims on Appeal do not require PTH in the bidomain peptide or protein. Therefore, claims 14-20 of the ‘609 patent do not anticipate claims 1-5 of the present application.

Furthermore, claims 14-20 of the ‘609 patent teach away from modifications that would replace the PTH recited in the claims with a growth factor, and remove the enzymatic degradation site. As stated in the Appeal Brief and above, such a modification is impermissible (*see* Appeal Brief, page 13). First, such a modification would materially change the mode of operation of matrix and method defined by claims 14-20 of the ‘609 patent (*see* MPEP §2143.01(V) and (VI)) since the degradation site allows for more specific release of PTH from the matrix (*see* the ‘609 patent at least at col. 14, lines 24-26 and 35-40). Second, such a modification would make the matrix defined by claim 14 of the ‘609 patent unsuitable for its intended purpose. By removing the enzymatic degradation site, a defined cleavage site for the release of an active factor is not present in the fusion peptide. Thus, in the case of a fusion peptide containing PTH that does not contain an enzymatic degradation site, a variety of PTH variants can result from enzyme activities, depending on (i) the enzymes present at the wound site, (ii) the density of the matrix, *i.e.* the accessibility of the covalently linked PTH and/or (iii) the amino acid sequence of the transglutaminase substrate domain. Thus, claims 14-20 of the

'609 patent teach away from a modification that involves removing the enzyme degradation site required by the claims.

The Examiner's also bases his rejection on use of the term "comprising" in the independent claims (Examiner's Answer, page 7, para. 4). However, the claims must be read as a whole. For example, regarding the importance of proper claim interpretation in an obviousness-type double patenting analysis, the Federal Circuit stated "it is important to bear in mind that comparison can be made only with what invention is *claimed* in the earlier patent, paying careful attention to the rules of claim interpretation to determine what invention a claim *defines* and not looking to the claim for anything that happens to be mentioned in it as though it were a prior art reference" (*General Foods Corp v. Studiengesellschaft Kohle mbH*, 972 F. 2d 1272, 1280 (Fed Cir. 1992)). The composition defined by claims 1-5 of the present application is structurally different from the matrix defined by claims 14-20 of the '609 patent, when the claims are read as a whole. Since claims 14-20 of the '609 patent require a fusion peptide that with PTH in one domain and an enzymatic degradation site between the first and second domains, it would not be obvious to one of ordinary skill in the art to structurally modify the fusion peptide by replacing the PTH with a growth factor and removing the enzymatic degradation site. For at least the reasons in the Appeal Brief and those discussed herein, claims 1-5 of the present application are not obvious over claims 14-20 of the '609 patent.

Claims 7 and 9 of the present application

For at least set forth in the Appeal Brief and above with respect to claims 1-5, claims 14-20 of the '609 patent do not make obvious claims 7 and 9 of the present application.

Claims 10-14 and 16-17 of the present application

For at least set forth in the Appeal Brief and above with respect to claims 1-5, claims 14-20 of the '609 patent do not make obvious claims 10-14 and 16-17 of the present application.

Claims 18-22 of the present application

For at least set forth in the Appeal Brief and above with respect to claims 1-5, claims 14-20 of the '609 patent do not make obvious claims 18-22 of the present application.

Claims 26 and 27 of the present application

For at least set forth in the Appeal Brief and above with respect to claims 1-5, claims 14-20 of the '609 patent do not make obvious claims 26 and 27 of the present application.

Claims 28-30 of the present application

For at least set forth in the Appeal Brief and above with respect to claims 1-5, claims 14-20 of the '609 patent do not make obvious claims 28-30 of the present application.

Claims 34 and 35 of the present application

For at least set forth in the Appeal Brief and above with respect to claims 1-5, claims 14-20 of the '609 patent do not make obvious claims 34 and 35 of the present application.

(d) Pending application No. 10/323,046 to Hubbell, et al. (the '046 application)

Claims 1-5, 7, 9-14, 16-22, 26-30, 34, and 35 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting in view of claims 1, 3-6, 9, 13, 14, 16-19, and 22-25 of the '046 application. Appellants respectfully traverse this rejection for at least the reasons set forth in the Appeal Brief and below.

(ii) Claims 1-5, 7, 9-14, 16-22, 26-30, 34 and 35 are not obvious in view of claims 1, 3-6, 9, 13, 14, 16-19, and 22-25 of the '046 application

(a) The Scope of Claims 1, 3-6, 9, 13, 14, 16-19, and 22-25 of the '046 application

Claims 1, 3-6, 9, 13, 14, 16-19, and 22-25 of the '046 application were summarized in the Appeal Brief (Appeal Brief, page 19). Furthermore, independent claims 1 and 13 were amended on October 21, 2008, to delete "bioactive factor" from the list of materials in the first domain of the fusion protein.

(b) Differences between claims 1, 3-6, 9, 13, 14, 16-19, and 22-25 of the '046 application and claims 1-5, 7, 9-14, 16-22, 26-30, 34, and 35 of the present application.

As noted in the Appeal Brief, the claims in the '046 application require an enzymatic or hydrolytic cleavage site between the first and second domains of the bidomain peptide. In contrast, none of the pending claims of the present application require a hydrolytic or enzymatic degradation cite between the first and second domains.

The Examiner points out that “comprising” language is used in the claims of the present application (Examiner’s Answer, page 8). However, as noted above with respect to the obviousness-type double patenting rejection over claims 14-20 of the ‘609 patent, one must read the claims as a whole to determine their proper scope. One cannot simply read into the claims of the present application a limitation that is not recited by the claims. Further, it would not be obvious to one of ordinary skill in the art to modify the claims in the ‘046 application to remove the requirement of an enzymatic or hydrolytic cleavage site. As noted in the Appeal Brief, such a modification of the claims in the ‘046 application would change principle of operation of the claims in the ‘046 application (*see* MPEP § 2143.01 (V)). Thus, for at least the reasons set forth in the Appeal Brief and above, 1, 3-6, 9, 13, 14, 16-19, and 22-25 of the ‘046 application do not make obvious claims 1-5, 7, 9-14, 16-22, 26-30, 34, and 35 of the present application.

Appellants further note that this is a provisional rejection since the claims in the ‘046 application are still undergoing prosecution.

For the at least the reasons set forth in the Appeal Brief and above, Appellants submit that claims 1-5, 7, 9-14, 16-22, 26-30, 34, and 35 are patentable.

Respectfully submitted,

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